UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

AUG 27 1987

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Registration of Tempo™ 2 (containing Cyfluthrin) and Risk Assessment of Pest Control Officer (PCO) Use in Buildings.

EPA No. 3125-GTE
Record No. 194578

Project No. 7-0680
Tox. Chem. No. 266E

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John E Whalan 8-18-87

THRU: Edwin R. Budd, Section Head
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Budd 8/19/87

Mobay Chemical Corporation has requested the registration of Tempo™ 2 Insecticide for use by pest control operators (PCO's) and professional applicators in buildings, and certain other sites. At the request of Registration Division, the Exposure Assessment Branch (EAB) prepared PCO and resident exposure estimates (L. Lewis memorandum, March, 16, 1987, attached). This memorandum will deal with these exposure estimates and the proposed registration of the product for PCO use.

The Baythroid products have gone through many name and formulation changes. According to the Registrant, the following names are for the same product:

Tempo 2 (the current name)
Baythroid 240 (not to be confused with Baythroid 240 EC)
Baythroid C 2 EC
* Baythroid 240 EC Formulation C

No new studies were submitted for this registration action. Instead, the battery of acute studies submitted for Baythroid 240 Ornamental Pyrethroid Insecticide (John Whalan memorandum; EPA No. 3125-GLE; August 18, 1986) are to suffice. These studies were performed using Baythroid C 2 EC and Baythroid

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* An eye irritation study was performed using Baythroid 240 EC Formulation C. Glenn Brussell, Mobay's Manager of Registration Research and Development informed Christine Dively (Registration Division) that "Baythroid 240 EC Formulation C" is identical to "Baythroid C 2 EC." He agreed to verify this statement in writing. To date, Toxicology Branch has not seen it.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

240 EC Formulation C, which are reportedly very similar to Tempo 2 (Baythroid 240). As shown below, the formulations for Baythroid C 2 EC and Tempo 2 are similar. The differences in formulations are minor, and not toxicologically significant.

	Baythroid C 2 EC	Tempo 2	
Baythroid Technical (92%)	24.3	26.51	active ingredient
[redacted]			

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The following table summarizes the status of the toxicity data base available to support the proposed registration:

	Cyfluthrin Technical Available	Tempo 2 Available
Acute oral toxicity	yes	yes
Acute dermal toxicity	yes	yes
Acute inhalation toxicity	yes	yes
Primary dermal irritation	yes	yes
Primary eye irritation	yes	yes
Dermal sensitization	yes	yes
21-day dermal	yes	
21-day inhalation	yes	
90-day subchronic inhalation	yes	
Teratology (2 species)	yes	
Reproduction	yes	
Chronic feeding (1 species)	yes	
Oncogenicity (2 species)	yes	
Metabolism	yes	
Mutagenicity	yes	
Special - "nervous system"	yes	

The proposed label (attached), states that, "Tempo 2 is intended for use by Professional Applicators for pest control in and around buildings and structures and their immediate surroundings and on modes of transport. Permitted areas of use include, but are not limited to, apartment buildings, greenhouses, hospitals, hotels, houses, industrial buildings, laboratories, manufacturing establishments, mausoleums, nursing homes, restaurants, schools, stores, warehouses and on aircraft, buses, rail cars, truck and trailers, vessels, and non-food areas of food handling establishments." The product is to be applied as a general, spot surface application, crack and crevice treatment, and pantry and premise pest control.

Many of the uses, such as hospitals, nursing homes, schools, restaurants, and food handling establishments may pose special exposure scenarios not discussed in the EAB document (that document dealt solely with PCO use in apartments and subsequent exposures of residents). It is also not clear to the Toxicology Branch that PCO use in apartments will necessarily represent a "worst case" exposure scenario for the many uses listed on the label. The Toxicology Branch yields to the Registration Division on this matter.

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One of the uses mentioned in the label, greenhouses, was addressed two years ago in a Toxicology Branch memorandum (John Whalan, EPA No. 3125-GLE, March 12, 1985). Toxicology Branch requested an exposure estimate from EAB for that use. In response to that memorandum, EAB requested the applicant to submit a greenhouse study (instead of using surrogate data). The Toxicology Branch cannot address the greenhouse use at this time since it has not received EAB's evaluation.

The label signal word and precautionary statements are acceptable and appropriate for a Category II hazard, based on the eye irritation study.

The following label changes are recommended (based on 40 CFR Parts 156 and 167):

1. The "Statements of Practical Treatment" should be modified since Tempo 2 contains >10% aromatic petroleum distillate. The component should be identified, and appropriate practical treatment supplied.

2. On the basis of the PCO risk assessment (attached), it is recommended that the following statement be added to the label:

   "Wear a respirator jointly approved by the Mine Safety and Health Administration and the National Institute for Occupational Safety and Health for pesticide application."

The Toxicology Branch has no objection to this registration provided Registration Division is satisfied that the concerns mentioned in this memorandum are not a problem. A Summary of selected toxicology data for cyfluthrin is attached.

TEMPO ™ 2 RISK ASSESSMENT

PCO Use and Resident Exposure In Buildings

In response to a conversation with Christine Dively (RD), this risk assessment includes exposure to PCO's by the dermal and inhalation routes. This memorandum will address these two routes on the basis of the available toxicity data base. It will be further expanded to include inhalation exposure to residents using the buildings following treatment by PCO's. Dermal exposure to residents will not be addressed because EAB explained that, "a method is not available to estimate dermal exposure of residents of treated houses from wipe tests."

The EAB memorandum described hand-pressurized or power-operated spray application by PCO's to buildings and structures and their immediate surroundings, and on modes of transport. The product is to be applied as a general, spot surface application, crack and crevice treatment, and pantry and premise pest control.

EAB assumed that a PCO will be wearing goggles or a face shield, a long-sleeved shirt and long pants, and may or may not be wearing protective gloves. Fifty percent of the cyfluthrin (based on surrogate data) will penetrate the PCO's clothing. There was no estimate of the daily duration of exposure, nor of the number of days that the PCO may be exposed. For the purpose of this risk assessment, the length of exposure is assumed by the Toxicology Branch to be similar to that in the appropriate animal studies.

EAB assumed that residents of the sprayed structures will be exposed for 15 hours/day. Some residents, such as children and compromised hospital patients may be more sensitive to the toxic effects of cyfluthrin. It is also presumed that cyfluthrin will be sprayed periodically, but there was no information as to the frequency of application.

In order to determine margins of safety by the dermal and inhalation routes, the following animal NOEL's for these routes were used:

Route	Type of Study	NOEL
PCO's -		
Inhalation	21-Day - Rat	0.0014 mg/l/day
Inhalation	90-Day - Rat	0.00009 mg/l/day
Dermal	21-Day - Rabbit	>250 mg/kg/day (HDT)
Residents -		
Inhalation	21-Day - Rat	0.0014 mg/l/day

Actual human exposure data for cyfluthrin were not used. Instead, data for other chemicals served as surrogate. The margin of safety calculations were not adjusted for interspecies pharmacodynamic differences. Based on the EAB supplied surrogate values, the margins of safety were as follows:

Margins of Safety

	Inhalation	Dermal
PCO's (21 day) =	296	329
PCO's (90 day) =	19.1	-
Residents (day 1) =	5110	-
(day 2) =	12,348	-
(day 3) =	49,392	-

Using a safety factor criteria of $\geq$100, the margin of Safety for PCO's by the inhalation route for a period of 90 days is not acceptable (MOS = 19.1). The use of a respirator is recommended as an easy way to increase safety. PCO inhalation exposure over a three week period is within the realm of acceptable risk (MOS = 296). Resident inhalation exposure is not a problem (MOS = 5110-49,392), although consideration should be given to populations that may be at particular risk. PCO dermal exposure is also not a problem (MOS = 329).

The following pages present the margin of safety calculations.

INHALATION EXPOSURE - PCO USE (90-Day Exposure)

Animal data:

90-Day rat inhalation NOEL = 0.00009 mg/l/day [a]

Assumptions:

Inhaled material is equally absorbed by rats and humans.
Rat minute volume (MV) = 0.0735 l/min [b]
PCO inhalation exposure = 0.0005 mg/kg/6 hr day [c]

Margin of Safety (MOS) Calculation:

- Rat NOEL x rat MV x 360 min/exposure = rat dose/6 hr exposure

  0.00009 mg/l/day x 0.0735 l/min x 360 min/exposure = 0.00238 mg/6 hr exposure

- $\frac{\text{mg/6 hr exposure}}{\text{kg rat body weight}}$ = mg/kg/6 hr exposure -

  $\frac{0.00238 \text{ mg/6 hr exposure}}{0.25 \text{ kg rat}}$ = 0.00953 mg/kg/6 hr exposure

- $\frac{\text{Rat NOEL (mg/kg/6 hr exposure)}}{\text{PCO dose (mg/kg/6 hr exposure)}}$ = Margin of Safety -

  $\frac{0.00953 \text{ mg/kg/6 hr exposure}}{0.0005 \text{ mg/kg/6 hr exposure}}$ = 19.1 = Margin of Safety

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[a] This rat NOEL is based on an inhalation regimen of 6 hrs/day, 5 days/week, for 13 weeks. The LEL in this study, 0.00071 mg/l/day, is based on findings of unthriftiness, unkempt fur, lethargy, and increased urinary protein.

[b] This value is from Reference-Handbook of Biological Data, W.S. Spector (Ed.), W.B. Saunders, Publisher, Philadelphia, Penn., 1964, p.220.

[c] This value is from the EAB review (page 9), and is based on surrogate data (chlorpyrifos). The EAB review did not mention the length of daily exposure, but it is assumed to be close to the 6 hour/day rat exposure.

INHALATION EXPOSURE - PCO USE (21-Day Exposure)

Animal data:

21-Day rat inhalation NOEL = 0.0014 mg/l/day [a]

Assumptions:

Inhaled material is equally absorbed by rats and humans.
Rat minute volume (MV) = 0.0735 l/min [b]
PCO inhalation exposure = 0.0005 mg/kg/6 hr day [c]

Margin of Safety (MOS) Calculation:

- Rat NOEL x rat MV x 360 min/exposure = rat dose/6 hr exposure

  0.0014 mg/l/day x 0.0735 l/min x 360 min/exposure = 0.0370 mg/6 hr exposure

- $\frac{\text{mg/6 hr exposure}}{\text{kg rat body weight}}$ = mg/kg/6 hr exposure -

  $\frac{0.0370 \text{ mg/6 hr exposure}}{0.25 \text{ kg rat}}$ = 0.1482 mg/kg/6 hr exposure

- $\frac{\text{Rat NOEL (mg/kg/6 hr exposure)}}{\text{PCO dose (mg/kg/6 hr exposure)}}$ = Margin of Safety -

  $\frac{0.1482 \text{ mg/kg/6 hr exposure}}{0.0005 \text{ mg/kg/6 hr exposure}}$ = 296 = Margin of Safety

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[a] This rat NOEL is based on an inhalation regimen of 6 hrs/day, 5 days/week, for 3 weeks. The LEL in this study, 0.0023 mg/l/day, is based on decreased body weight gain.

[b] This value is from Reference-Handbook of Biological Data, W.S. Spector (Ed.), W.B. Saunders, Publisher, Philadelphia, Penn., 1964, p.220.

[c] This value is from the EAB review (page 9), and is based on surrogate data (chlorpyrifos). The EAB review did not mention the length of daily exposure, but it is assumed to be close to the 6 hour/day rat exposure.

INHALATION EXPOSURE - RESIDENT

Animal data:

21-Day rat inhalation NOEL = 0.0014 mg/l/day [a]
21-Day rat inhalation NOEL adjusted for 15 hour exposure = 0.00056 mg/l/day[b]

Assumptions:

Inhaled material is equally absorbed by rats and humans.
Rat minute volume (MV) = 0.0735 l/min [c]
Resident inhalation exposure - DAY 1 = 0.000029 mg/kg/15 hr day [d]
DAY 2 = 0.000012 mg/kg/15 hr day [d]
DAY 3 = 0.000003 mg/kg/15 hr day [d]

Margin of Safety (MOS) Calculation:

- Rat NOEL x rat MV x 900 min/exposure = rat dose/15 hr exposure

  0.00056 mg/l/day x 0.0735 l/min x 900 min/exposure = 0.0370 mg/15 hr exposure

- $\frac{\text{mg/15 hr exposure}}{\text{kg rat body weight}}$ = mg/kg/15 hr exposure -

  $\frac{0.0370 \text{ mg/15 hr exposure}}{0.25 \text{ kg rat}}$ = 0.1482 mg/kg/15 hr exposure

- $\frac{\text{Rat NOEL (mg/kg/15 hr exposure)}}{\text{Resident dose (mg/kg/15 hr exposure)}}$ = Margin of Safety -

  DAY 1 - $\frac{0.1482 \text{ mg/kg/15 hr exposure}}{0.000029 \text{ mg/kg/15 hr exposure}}$ = 5110 = Margin of Safety

  DAY 2 - $\frac{0.1482 \text{ mg/kg/15 hr exposure}}{0.000012 \text{ mg/kg/15 hr exposure}}$ = 12,348 = Margin of Safety

  DAY 3 - $\frac{0.1482 \text{ mg/kg/15 hr exposure}}{0.000003 \text{ mg/kg/15 hr exposure}}$ = 49,392 = Margin of Safety

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[a] This rat NOEL is based on an inhalation regimen of 6 hrs/day, 5 days/week, for 21 days. According to the surrogate data from EAB, cyfluthrin applied to structures will dissipate appreciably over several days. For this reason, the 21-day rat NOEL was used instead of the 90-day rat NOEL.

[b] The rat NOEL was divided by a factor of 2.5 to compensate for the difference in exposure times for resident and rat (i.e., 15 hr/6 hr = 2.5).

[c] This value is from Reference-Handbook of Biological Data, W.S. Spector (Ed.), W.B. Saunders, Publisher, Philadelphia, Penn., 1964, p.220.

[d] These values are from the EAB review (page 9), and are based on surrogate data (dichlorvos).

DERMAL EXPOSURE - PCO USE

Animal data:

21-Day rabbit dermal NOEL >250 mg/kg/day

Assumptions:

Dermally applied material is absorbed equally by rabbits and humans.
PCO dermal exposure (with or without gloves) = 0.760 mg/kg/day

Margin of Safety (MOS) Calculation:

- $\frac{\text{Rabbit NOEL}}{\text{Estimated PCO exposure}}$ = Margin of Safety -

$$\frac{250 \text{ mg/kg/day}}{0.760 \text{ mg/kg/day}} = 329 = \text{Margin of Safety}$$